

We Claim:

1. In a method to modulate exogenous gene expression comprising contacting an ecdysone receptor complex comprising:

- 5 a) a DNA binding domain;
- b) a ligand binding domain;
- c) a transactivation domain; and
- d) a ligand;

with a DNA construct comprising:

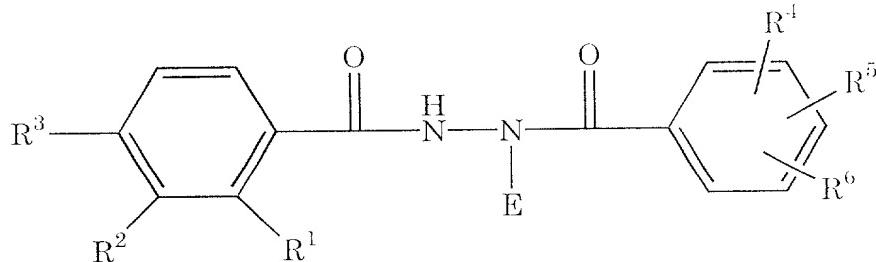
- a) the exogenous gene; and
- 10 b) a response element;

wherein:

- a) the exogenous gene is under the control of the response element; and
- b) binding of the DNA binding domain to the response element in the presence of the ligand results in activation or suppression of the gene;

the improvement comprising:

selecting the ligand from a compound of the formula:



wherein:

E is a (C₄-C₆)alkyl containing a tertiary carbon or a cyano(C₃-C₅)alkyl

20 containing a tertiary carbon;

R¹ is H, Me, Et, i-Pr, F, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe,

OEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH,

OMe, OEt, O-n-Pr, OAc, NMe₂, NET₂, SMe, SET, SOCF₃, OCF₂CF₂H,

COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr,

SCN, SCHF₂, SOMe, NH-CN, or joined with R¹ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrosuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

- 5 R³ is H, Et, or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrosuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

10 R⁴, R⁵, and R⁶ are independently H, Me, Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SET;

provided that:

- a) when R¹ is Me and R² is OMe;

then R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;

- b) when R¹ is Me and R² is OEt;

then R³ is H and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl;

- c) when R¹ is Et and R² is OMe or OEt;

then R³ is H and the combination R⁴, R⁵, and R⁶ is:

i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or

ii) R⁶ is H, R¹ is Me, and R⁵ is Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe,

25 OEt, SMe, or SET;

- d) when R¹ is 1-Pr;

then R² is OMe, or OEt; R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;

- e) when R³ is Et;

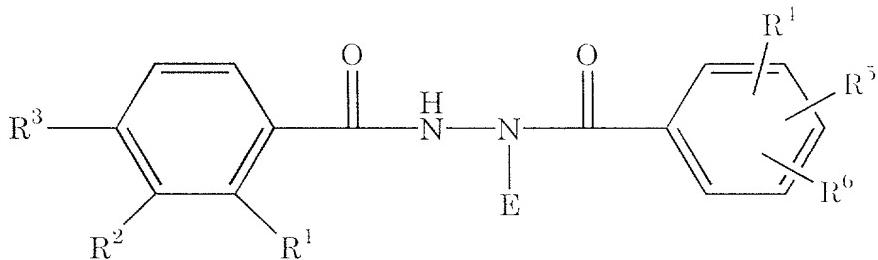
30 then R² is H, R¹ is F or Cl, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;

- f) when R² and R³, together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;
then R¹ is Me or Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- g) when R² and R³, together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyrryl ring;
then R¹ is Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- 5 h) when R¹ is formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe,
CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl,
CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;
10 then R² is OMe or OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me; and
- i) when R² is Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl,
CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac,
F, Cl, OH, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SET, SOCF₃, OCF₂CF₂H, COEt,
cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN,
SCHF₂, SOMe, or NH-CN;
then R¹ is Et, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.

2. A method to modulate exogenous gene expression comprising contacting an

20 ecdisone receptor complex comprising:

- a) a DNA binding domain;
b) a ligand binding domain;
c) a transactivation domain; and
d) a ligand of the formula:



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wherein:

E is a (C₁-C₆)alkyl containing a tertiary carbon or a cyano(C₃-C₅)alkyl containing a tertiary carbon;

R¹ is H, Me, Et, i-Pr, F, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SET, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, NH-CN, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrafuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R³ is H, Et, or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrafuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R⁴, R⁵, and R⁶ are independently H, Me, Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SET;

provided that:

a) when R¹ is Me and R² is OMe;

then R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;

b) when R¹ is Me and R² is OEt;

then R³ is H and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl;

c) when R¹ is Et and R² is OMe or OEt;

then R³ is H and the combination R⁴, R⁵, and R⁶ is:

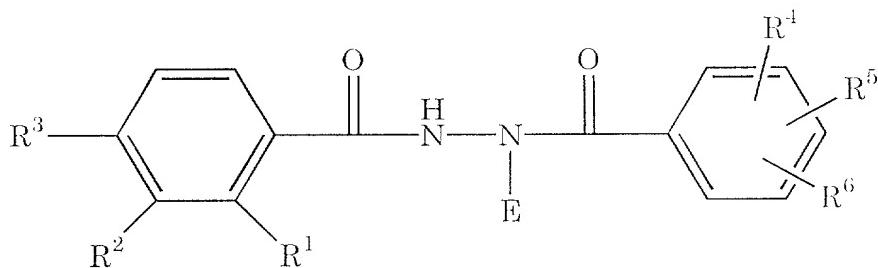
- 1) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or
- 5 ii) R⁶ is H, R⁴ is Me, and R⁵ is Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;
- d) when R¹ is i-Pr;
- 10 then R² is OMe, or OEt; R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- e) when R³ is Et;
- 15 then R² is H, R¹ is F or Cl, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- f) when R² and R³, together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;
- then R¹ is Me or Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- g) when R² and R³, together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring,
- then R¹ is Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- h) when R¹ is formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;
- 20 then R² is OMe or OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me; and
- i) when R² is Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe₂, NET₂, SMe, SEt, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, or NH-CN;
- 25 then R¹ is Et, R³ is H, the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- with a DNA construct comprising:
- 30 a) the exogenous gene; and
- b) a response element;

wherein:

- a) the exogenous gene is under the control of the response element; and
- b) binding of the DNA binding domain to the response element in the presence of the ligand results in activation or suppression of the gene.

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3. A method to modulate the expression of one or more exogenous genes in a subject, comprising administering to the subject an effective amount of a ligand of the formula:



wherein:

E is a (C₄-C₆)alkyl containing a tertiary carbon or a cyano(C₃-C₅)alkyl containing a tertiary carbon;

R¹ is H, Me, Et, i-Pr, F, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SET, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, NH-CN, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

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R³ is H, Et, or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the

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oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R¹, R⁵, and R⁶ are independently H, Me, Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

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provided that:

a) when R¹ is Me and R² is OMe;

then R³ is H; and the combination R¹, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;

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b) when R¹ is Me and R² is OEt;

then R³ is H and the combination R¹, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl;

c) when R¹ is Et and R² is OMe or OEt;

then R³ is H and the combination R¹, R⁵, and R⁶ is:

- i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or
- ii) R⁶ is H, R⁴ is Me, and R⁵ is Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

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d) when R¹ is i-Pr;

then R² is OMe, or OEt; R³ is H; and the combination R¹, R⁵, and R⁶ is 3,5-di-Me;

e) when R³ is Et;

then R² is H, R¹ is F or Cl, and the combination R¹, R⁵, and R⁶ is 3,5-di-Me;

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f) when R² and R³, together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;

then R¹ is Me or Et and the combination R¹, R⁵, and R⁶ is 3,5-di-Me;

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g) when R² and R³, together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring;

then R¹ is Et and the combination R¹, R⁵, and R⁶ is 3,5-di-Me;

h) when R¹ is formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

then R² is OMe or OEt, R³ is H, and the combination R¹, R⁵, and R⁶ is 5
3,5-di-Me; and

- 1) when R² is Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, or NH-CN;
- then R¹ is Et, R³ is H, the combination R¹, R⁵, and R⁶ is 3,5-di-Me;

wherein the cells of the subject contain:

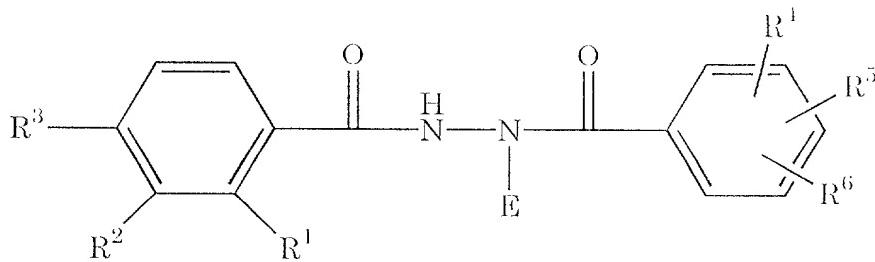
- a) an ecdysone receptor complex comprising:
- 1) a DNA binding domain;
 - 2) a binding domain for the ligand; and
 - 3) a transactivation domain; and
- b) a DNA construct comprising:
- 1) the exogenous gene; and
 - 2) a response element; and

wherein:

- a) the exogenous gene is under the control of the response element; and
- b) binding of the DNA binding domain to the response element in the presence of the ligand results in activation or suppression of the gene.

25 4. A method for producing a polypeptide comprising the steps of:

- a) selecting a cell which is substantially insensitive to exposure to a ligand of the formula:



wherein:

E is a (C₄-C₆)alkyl containing a tertiary carbon or a cyano(C₃-C₅)alkyl containing a tertiary carbon;

R¹ is H, Me, Et, i-Pr, F, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SET, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, NH-CN, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R³ is H, Et, or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R⁴, R⁵, and R⁶ are independently H, Me, Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SET;

provided that:

a) when R¹ is Me and R² is OMe;

then R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;

b) when R¹ is Me and R² is OEt;

then R³ is H and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl;

c) when R¹ is Et and R² is OMe or OEt;

then R³ is H and the combination R⁴, R⁵, and R⁶ is:

i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or

ii) R⁶ is H, R⁴ is Me, and R⁵ is Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl,

OMe, OEt, SMe, or SET;

d) when R¹ is i-Pr;

then R² is OMe, or OEt; R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;

e) when R³ is Et;

then R² is H, R¹ is F or Cl, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;

f) when R² and R³, together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;

then R¹ is Me or Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;

g) when R² and R³, together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring;

then R¹ is Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;

h) when R¹ is formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂:

then R² is OMe or OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me; and

i) when R² is Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SET, SOCF₃, OCF₂CF₂H,

COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, or NH-CN;

then R¹ is Et, R³ is H, the combination R¹, R⁵, and R⁶ is 3,5-di-Me;

b) introducing into the cell:

5 1) a DNA construct comprising:

- a) an exogenous gene encoding the polypeptide; and
- b) a response element;

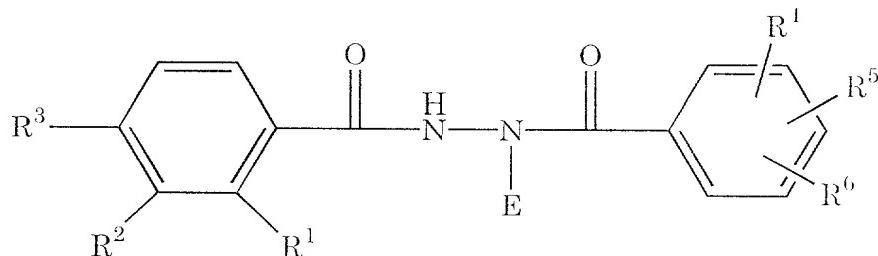
wherein the gene is under the control of the response element; and

10 2) an ecdysone receptor complex comprising:

- a) a DNA binding domain;
- b) a binding domain for the ligand; and
- c) a transactivation domain; and

c) exposing the cell to the ligand.

5. A method for regulating endogenous or heterologous gene expression in a transgenic organism comprising contacting a ligand of the formula:



wherein:

E is a (C₄-C₆)alkyl containing a tertiary carbon or a cyano(C₃-C₅)alkyl containing a tertiary carbon;

R¹ is H, Me, Et, i-Pr, F, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl,

25 Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SET, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, NH-CN, or joined with R³ and the

phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

5 R³ is H, Et, or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

10 R⁴, R⁵, and R⁶ are independently H, Me, Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SET;

provided that:

a) when R¹ is Me and R² is OMe;

then R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;

b) when R¹ is Me and R² is OEt;

then R³ is H and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl;

c) when R¹ is Et and R² is OMe or OEt;

then R³ is H and the combination R⁴, R⁵, and R⁶ is:

i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or

ii) R⁶ is H, R⁴ is Me, and R⁵ is Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SET;

d) when R¹ is i-Pr;

then R² is OMe, or OEt; R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;

e) when R³ is Et;

then R² is H, R¹ is F or Cl, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;

- f) when R² and R³, together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;
then R¹ is Me or Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- g) when R² and R³, together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring;
then R¹ is Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- 5 h) when R¹ is formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;
then R² is OMe or OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me; and
- i) when R² is Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe₂, NET₂, SMe, SET, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOME, or NH-CN;
then R¹ is Et, R³ is H, the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
with an ecdysone receptor complex within the cells of the organism wherein
the cells further contain a DNA binding sequence for the ecdysone
receptor complex when in combination with the ligand and wherein
formation of an ecdysone receptor complex-ligand-DNA binding sequence
complex induces expression of the gene.
6. The method of Claim 2 wherein the lgand is of the specified formula and E is t-butyl; R¹ is Me, Et, i-Pr, or F; R² is OH, OMe, OEt, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R³ is H, Et or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R⁴, R⁵, and R⁶ are independently Me, F, Cl, CH₂OH, or
20 OMe.
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7. The method of Claim 3 wherein the ligand is of the specified formula and E is t-butyl; R¹ is Me, Et, i-Pr, or F; R² is OH, OMe, OEt, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R³ is H, Et or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R⁴, R⁵, and R⁶ are independently Me, F, Cl, CH₂OH, or OMe.
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8. The method of Claim 4 wherein the ligand is of the specified formula and E is t-butyl; R¹ is Me, Et, i-Pr, or F; R² is OH, OMe, OEt, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R³ is H, Et or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R⁴, R⁵, and R⁶ are independently Me, F, Cl, CH₂OH, or OMe.
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9. The method of Claim 5 wherein the ligand is of the specified formula and E is t-butyl; R¹ is Me, Et, i-Pr, or F; R² is OH, OMe, OEt, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R³ is H, Et or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R⁴, R⁵, and R⁶ are independently Me, F, Cl, CH₂OH, or OMe.
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10. The method of Claim 2 wherein the ligand is of the specified formula and E is t-butyl, R¹ is Et, R² is OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.
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11. The method of Claim 3 wherein the ligand is of the specified formula and E is t-butyl, R¹ is Et, R² is OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.
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12. The method of Claim 4 wherein the ligand is of the specified formula and E is t-butyl, R¹ is Et, R² is OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.
13. The method of Claim 5 wherein the ligand is of the specified formula and E is t-butyl, R¹ is Et, R² is OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.
14. The method of Claim 2 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.
15. The method of Claim 3 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.
16. The method of Claim 4 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.
17. The method of Claim 5 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.
18. The method of Claim 3 wherein the subject is a plant
19. The method of Claim 3 wherein the subject is a mammal.